Can too much exercise be dangerous: what can we learn from the athlete's heart?

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Key words

arrhythmias, atrial fibrillation, BJCA, exercise, heart diseases, sports, ventricular remodelling

First published online 2nd June 2021

doi: 10.5837/bjc.2021.030

Br J Cardiol 2021;**28**:95–7

Exercise prevents and aids treatment of coronary heart disease, hypertension, heart failure, diabetes mellitus, obesity and depression, reduces cardiac events and improves survival. However, evidence suggests that the relationship between exercise and mortality may be curvilinear, with modest additional benefit at higher levels. Intensive exercise has also been associated with increased atrial fibrillation risk, although its clinical implications are not well understood. Other proposed adverse effects of exercise on the heart, including reduced right ventricular function, elevated cardiac biomarkers, myocardial fibrosis and coronary artery calcification, are less substantiated. Current evidence cannot affirm that extreme exercise is dangerous and future studies should combine large cohorts to obtain a statistically reliable limit. Associations between features of the athlete's heart and cardiovascular morbidity and mortality should also be explored.

Introduction

With semi-professional sporting events becoming more accessible,[1] the effect of endurance training on the body is increasingly relevant, not just in elite athletes, but also fitness enthusiasts. Exercise prevents and aids treatment of coronary heart disease (CHD), hypertension, heart failure, diabetes mellitus, obesity and depression,[2,3] reduces cardiac events,[1] and improves survival.[4,5] However, there is concern excessive exercise could have adverse cardiac effects.[2] This article aims to address whether an upper limit to mortality benefits of exercise exists, consider physiological and potentially pathological changes in the athlete's heart, and discuss implications on exercise recommendation and future research. The dangers of sports in individuals with underlying rhythm and structural abnormalities, while important, are beyond the focus of this article.

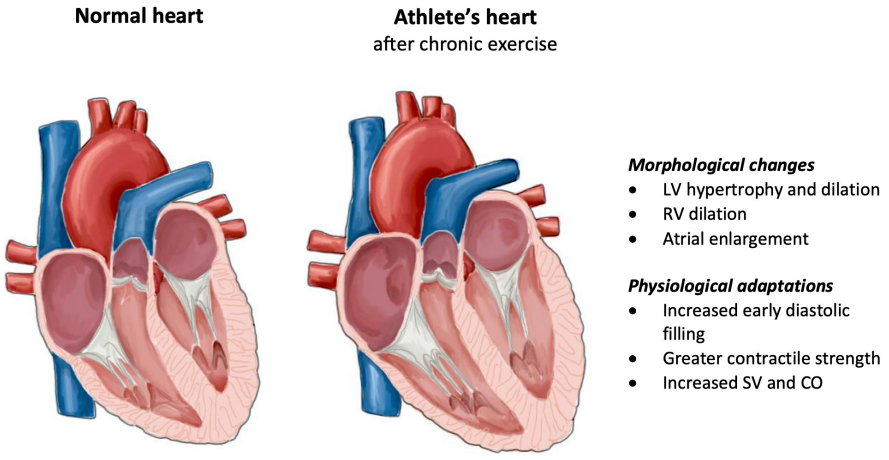
Exercise and mortality: is there an upper limit?

Physical activity (PA) improves all-cause and cardiovascular disease (CVD) mortality,[4,5] but evidence suggests dwindling gains at high levels (**table 1**).[5,6] A U-shaped dose-response curve between exercise and mortality was previously described, with progressive loss of benefit past an upper limit.[5] More recently, it appears this relationship may be curvilinear. Gain in mortality benefit was steepest at moderate PA (3–5 times recommendations) with modest additional benefit at higher levels, but no indication of harm even at 10 times the recommended level.[6] A small study presented at the American Heart Association (AHA) 2019 meeting found no CVD deaths in 66 athletes performing extreme exercise (≥10,000 metabolic equivalents of task [MET]-minutes/week).[7] In aggregate, there is presently no defined upper limit of mortality benefit from exercise.

The athlete's heart

Acute aerobic exercise can increase cardiac output (CO) by fourfold in healthy untrained individuals and eightfold in elite athletes, largely mediated by increased stroke volume (SV).[3] With chronic exercise (**figure 1**), exercise-induced cardiac remodelling (EICR) such as left ventricular (LV) hypertrophy and dilation of all cardiac chambers develops. These enhance diastolic filling and augment SV, further increasing CO and maximal oxygen uptake.[1,3] The athlete's electrocardiogram (ECG) differs from the general healthy population (e.g. benign arrhythmias, axis deviation, voltage criterion, ST changes) due to increased vagal tone and enlarged cardiac dimensions.[1] While physiological adaptations to exercise within certain

Figure 1. Visual representation of the morphological and physiological adaptations in the heart with chronic exercise



Key: CO = cardiac output; LV = left ventricle; RV = right ventricle; SV = stroke volume

Table 1. Overview of the impact of exercise on mortality and potential adverse effects on the heart as evidenced in current literature

Key findings	Relevant studies
All-cause mortality and CVD mortality	
• Greatest mortality benefit with moderate exercise and decreasing benefit at higher levels	Schnohr *et al.* (2013)[5] Arem *et al.* (2015)[6]
• No evidence of harm even at extreme levels of exercise	Arem *et al.* (2015)[6] DeFina *et al.* (2019)[7]
Ventricular function	
• Transient RV enlargement and reduced systolic function associated with intensive exercise • Elevated cardiac enzymes corresponding to exercise duration and magnitude of reduction in RV function	La Gerche *et al.* (2014)[8]
Myocardial fibrosis	
• LGE found in 5.9% of 30 studied athletes • Varying LGE patterns and locations may suggest myocardial fibrosis occurs in those with underlying cardiac disease	van de Schoor *et al.* (2016)[9]
Atrial fibrillation	
• Increased risk of AF associated with higher levels of exercise	Andersen *et al.* (2013)[10] Thelle *et al.* (2013)[11]
• Higher incidence of stroke in athletes with AF compared with non-athletes without AF • Among those with AF, athletes had lower stroke incidence and mortality compared with non-athletes	Svedberg *et al.* (2019)[14]
Coronary artery calcification	
• Greater CAC prevalence with increased exercise • Higher prevalence of calcified plaques and lower prevalence of mixed plaques compared with more sedentary counterparts	Aengevaeren *et al.* (2017)[12] Merghani *et al.* (2017)[13]

Key: AF = atrial fibrillation; CAC = coronary artery calcium; CVD = cardiovascular disease; LGE = late gadolinium enhancement; RV = right ventricle

parameters improves performance,[3] intensive exercise has been associated with reduced right ventricular (RV) function,[8] elevated cardiac biomarkers,[2] myocardial fibrosis,[9] atrial fibrillation (AF),[10,11] and coronary artery calcification (CAC).[12,13] These are discussed below and key study findings summarised in **table 1**.

Remodelling and ventricular function

EICR may be difficult to distinguish from pathology, and some athletes have cardiac dimensions exceeding pathological thresholds.[1] Further, some propose that not all EICR may be benign.[2] Intensive endurance exercise has been associated with RV enlargement and reduced systolic function, most pronounced after longer events and faster timings.[8] Although changes normalised within 6–11 days, it is unknown if repeated transient reduction in RV function, with inadequate myocardial recovery in between, may damage the heart in the long term.

Myocardial fibrosis

Myocardial fibrosis, measured as late gadolinium enhancement (LGE) on cardiac magnetic resonance (CMR) imaging, is present in some athletes (5.9% in a systematic review).[9] Location varies widely, but fibrosis was most frequently found near the interventricular septum and RV insertion points. Some speculate transient injury during exercise results in scarring.[9] Serological markers associated with damage (e.g. cardiac troponins, creatine kinase-MB, B-type natriuretic peptide) transiently rise during and after exercise,[2] and were found to correspond to reduced RV function.[8] However, it is unusual that myocardial fibrosis was detected in only a small proportion of athletes, considering most engaged in high PA. Certain individuals may be genetically susceptible and LGE pattern variation (non-specific, ischaemic, myocarditic and hypertrophic)[9] also raises the possibility that myocardial fibrosis occurs in those with underlying cardiac disease.[4]

Atrial fibrillation

Lower AF risk is seen with low-to-moderate exercise, but intensive PA may increase risk.[4] Elite skiers who participated in more races had increased AF incidence,[10] and highly active men were three times more likely to be prescribed flecainide, a surrogate

marker for lone AF, than sedentary men.[11] Clinical implications of AF in athletes are not completely understood, but a recent study found lower stroke and mortality incidence in skiers with AF compared with non-skiers with AF. Stroke risk was still higher, however, compared with non-skiers without AF.[14] Atrial enlargement and increased parasympathetic tone may contribute to AF in athletes.[2,14] There is currently no indication that chronic exercise promotes dangerous ventricular arrhythmias in those without underlying disease.[10]

Coronary artery calcification

CHD is the leading cause of exercise-related sudden cardiac death in older athletes (>35 years old).[1,4] CAC predicts atherosclerotic plaque burden and risk of adverse cardiovascular events.[12] Male athletes are more likely to have CAC than sedentary men and among athletes, increased lifelong exercise is associated with higher CAC prevalence.[12] However, athletes often have predominantly calcified plaques, whereas less active individuals usually have mixed plaques, which are associated with significantly higher cardiovascular risk.[12,13] Athletes have a lower CHD risk than non-athletes,[12] and the clinical significance of CAC in athletes remains unclear. It is possible exercise may facilitate plaque remodelling and confer stability.[4]

Moving forward

The AHA recommends at least 150–300 minutes of moderate or 75–150 minutes of vigorous aerobic PA weekly.[15] Arguably, a curvilinear relationship between exercise and mortality does not greatly change recommendations for the general population. Many engage in too little exercise and encouraging any level of PA is the priority. Indeed, exercise significantly improves survival, irrespective of amount, when compared with inactivity.[5,6] With the highest gains at the start of the dose-response curve, clinicians can be heartened that encouraging patients to begin exercising may confer the most benefit. For elite and highly active amateur athletes, there appears no immediate need to caution against excessive exercise from a mortality standpoint. Current evidence has yet to define an upper limit of benefit, with continued marginal gains even at PA 10 times the recommended level.[6] The proportion of individuals engaging in PA at the highest ends of the dose-response curve is small, therefore, future studies should combine large cohorts to obtain a statistically reliable limit. Well-controlled intervention studies are important to address confounders in observational data.

The association between high PA levels and AF potentially describes an adverse effect on the athlete's heart. While exercise may offset some stroke risk in athletes with AF, the risk is still higher compared with non-athletes without AF.[14] Risk stratification for anticoagulation is similar to non-athletes but management nuances should be explored.[4] The other propositions are less substantiated: long-term effects of transiently reduced RV function are uncertain, non-exercise-related underlying causes may contribute to myocardial fibrosis and the clinical implications of CAC in athletes are unknown. A series of insults from vigorous exercise in a susceptible individual may be harmful, but this should not form the basis on which to restrict exercise training.[4] Future studies should include longer follow-up for long-term effects, and explore associations between specific features of the athlete's heart and cardiovascular morbidity and mortality.

Conclusion

Current evidence cannot affirm that high levels of exercise are dangerous, although there is an indication of diminishing mortality benefit and increased AF risk. There is still much to learn about the athlete's heart, and clinicians should remain open to potential harms in order to fairly advise athletes aiming for sporting excellence. For the rest of us, as with nearly everything in medicine, exercise in moderation may be the wise approach

Key messages

- Exercise has significant health benefits, reduces cardiac events and improves survival. There may be diminishing mortality benefit at higher levels of exercise but an upper limit has yet to be defined
- High levels of exercise are associated with increased atrial fibrillation (AF) risk, although its clinical implications are not well understood. Risk stratification for anticoagulation is extrapolated from data from non-athletes, and nuances in the management of this specific group should be explored
- Intensive exercise may be associated with adverse structural and functional changes in the heart. However, their significance is unclear and further study is needed to explore their impact on cardiovascular morbidity and mortality

Conflicts of interest

None declared.

Funding

None.

Editors' note

This article was the prize-winning entry in the National Essay Prize 2020 of the British Junior Cardiologists' Association (BJCA).

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